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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/577,489	05/25/2000	Ray W. Wood	029318/0596	7761

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EXAMINER
QAZI, SABIHA NAIM

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 01/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/577,489	Applicant(s) WOOD ET AL.	
	Examiner Sabiha Qazi	Art Unit 1616	

-- Th MAILING DATE of this communication appears on th cover sh t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-46* is/are pending in the application.

4a) Of the above claim(s) *10-27, 46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Acknowledgement is made of the letter filed in paper no. 19. Claims 10-46 are pending. Claims 10-27 and 46 are withdrawn from consideration as non-elected invention. Claims 28-45 are rejected. No claim is allowed at the present time. Finality of the action is withdrawn as was requested by Applicants. Arguments filed in paper no. 19 were fully considered but are not found persuasive.

This Application claims CIP of 08/394,103 filed on Feb. 24, 1995, now abandoned.

Rejection of Claim 28 Under 35 U.S.C. 112, Second Paragraph

Applicants' arguments are found persuasive. Rejection of claim 28 under 35 USC 112, Second Paragraph is withdrawn because the claims are amended.

Rejection of Claims 28-45 Under 35 U.S.C. 112, First Paragraph

Claims 28-45 were rejected under 35 USC 112, First Paragraph, as lacking enablement on two grounds:

1) The claim limitation "liquid droplet" lacks support in the specification; and
2) The method steps in claim 28 were not disclosed.

- In claim 28, part (a), the Applicants intend to use a "liquid," which may be water or any other liquid. It is not the same as "liquid droplets." Applicants reference to "aqueous droplets" and "droplets of

an aqueous dispersion of nanoparticles" are correct. Water is enabled; liquid is not.

- The enablement for the method of claim 28 is not an issue. The issue is that the *steps* of the method as claimed in claim 28 are not disclosed. Method claims are required to have steps.
- The Examiner has responded to the arguments made by Applicant.

Rejection of Claims Under 35 U.S.C. 103(a)

Claims 28-45 were rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5747001 ("Weidmann et al.") and U.S. Patent No. 5145684 ("Liversedge et al.").

- The filing date of the parent application cannot be granted, as the subject matter as presently claimed was not found. The Applicants' Request for Clarification states that exemplary support for claimed benefit of priority can be found at, for example, page 3, lines 16-21; and page 4, lines 3-11 and 15-27 in Application 08/394,103.

For Applicants' convenience, the lines of exemplary support are posted below.

In accordance with the present invention, there is provided an aerosol comprising droplets of an aqueous dispersion of nanoparticles, said nanoparticles comprising

insoluble therapeutic or diagnostic agent particles having a surface modifier on the surface thereof. **(Page 3, Lines 16-21)**

In yet another embodiment, there is provided a method of diagnosing a mammal, said method comprising the steps of:

a) forming an aerosol of an aqueous dispersion of nanoparticles, said nanoparticles comprising insoluble diagnostic imaging agent particles having a surface modifier on the surface thereof;

b) administering said aerosol to the respitorary system of said mammal; and

c) imaging said imaging agent in said respiratory system. **(Page 4, Lines 3-12)**

The compositions of the invention are aerosols. Aerosols can be defined for the present purpose as colloidal systems consisting of very finely divided liquid droplets dispersed in and surrounded by a gas. The droplets in the aerosols typically have a size less than about 50 microns in diameter although droplets of a much smaller size are possible. **(Page 4, Lines 15-27)**

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i. Examiner could not find the particles to "have an average particle size of less than about 1000 nm." Examiner could not find "a liquid."

ii. Since Examiner cannot find "exemplary support" for the claimed invention in Application 08/394,103, the priority cannot be granted. Therefore, Weidmann et al. is still prior art.

iii. Therefore, the combination of Weidmann et al. with Liversidge et al. is still considered obvious to one of ordinary skill in the art to arrive at the claimed subject matter at the time of invention.

- Applicants are arguing that one of ordinary skill in the art at the time of claimed invention would not have been motivated to make an aerosol composition comprising the nanoparticulate active agent composition of Liversidge et al.

  Examiner reiterates that one of ordinary skill in the art at the time of claimed invention *would* have been motivated to arrive at the claimed subject matter at the time of invention because of the combined teachings of Weidmann et al. and Liversidge et al.

  - The arguments made about the teachings of Cameron et al., Nikander et al., and Tiano are irrelevant as Weidmann et al. is still considered to be prior art. With *the combined teaching* of Weidmann et al. and Liversidge et al, one of ordinary skill in the art at the

time of claimed invention would have been motivated to arrive at the claimed subject matter at the time of invention.

- The Examiner addresses all the arguments made by the Applicants.

- However, Examiner notes that the Applicants did not address the Double Patenting rejection over U.S. Patent No. 6264922 ("Wood et al.").

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double

patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 28-45 rejected under the judicially created doctrine of double patenting over claims 24-30 of US Patent No. 6264922 ("Wood et al.") and claims 1-10 of US Patent No. 5747001 ("Wiedmann et al.") since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows:

(a) Claims 24-30 of Wood et al. are drawn to a method of treating a mammal comprising delivering a composition of nanoparticles to lungs, a composition which is instantly claimed is considered obvious for delivering an aerosol containing nanoparticles.

(b) Claims 1-10 of Wiedmann et al. are drawn to a composition and method for forming an aerosol of an aqueous dispersion of nanoparticles, said nanoparticles comprising insoluble beclomethasone particles comprising:

a. providing an aqueous suspension of nanoparticles, wherein the nanoparticles comprise 0.1 to 60% (w/w) of insoluble beclomethasone particles having (1) an average particle size of less than about 400 nm, and (2) 0.1 to 90% (w/w) of a surface modifier

adsorbed on the surface thereof; and

b. nebulizing said suspension so as to form an aerosol.

Weidmann et al. is also drawn to a method of treating a respiratory related illness of a mammal comprising:

1. administering an effective amount of an aerosol comprising an aqueous dispersion of nanoparticles, wherein said nanoparticles comprise 0.1 to 60% (w/w) of insoluble beclomethasone particles having (1) an average particle size of less than about 400 nm, and (2) 0.1 to 90% of a surface modifier adsorbed on the surface thereof, wherein droplets of the aerosol deposit in the respiratory tract of the mammal.

Instant claims are considered obvious over the cited references for the reasons cited below.

Furthermore, there is no apparent reason why applicant was prevented from presenting claims corresponding to those of the instant application during prosecution of the application, which matured into a patent. See MPEP § 804.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 28-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5747001 ("Wiedmann et al."), US 6264922 ("Wood et al."), and US 5145684 ("Liversidge et al."). All of the references cited teach a composition that embraces Applicant's claimed invention.

See lines 20-67, col. 2, in Wiedmann et al., where an aerosol comprising nanoparticles of beclomethazone dipropionate having surface modifier on the surface, for administering to the respiratory system is taught. See also lines 5-67, col. 3 and lines 1-67 in col. 4 where surface modifiers are listed.

Weidmann et al. teaches the particle size less than 400 nm, whereas instant invention claims less than 1000 nm. See entire document, especially Tables I-III in col. 14, claims, and examples.

Liversidge et al. teaches that commercial airjet milling techniques provide particles ranging in average particle size from as low as 1,000 to 50,000 nm (1 to 50 microns). The reference also teaches crystalline drug particle having a surface modifier adsorbed on the surface thereof in an amount sufficient to maintain an effective particle size of less than 400 nm. See the entire document, especially lines 47-50 in col. 1, claims, and examples.

Wood et al.'s claim 24 teaches a method of treating a mammal in need comprising delivering nanoparticles to the lungs of the mammal, wherein said method comprises the steps of:

(a) forming a nebulized aerosol of an dispersion of liquid droplets, wherein the aerosol is useful for delivery of the nanoparticles to the lungs of a mammal, wherein:

(i) the liquid droplets have a particle size of less than about ten microns in diameter;

(ii) the liquid droplets consist essentially of a liquid, a crystalline therapeutic agent, and at least one surface modifier; and

(iii) the aerosol is useful for delivery of the nanoparticles to the lungs of a mammal; wherein said nanoparticles consist essentially of:

(1) crystalline particles of a therapeutic agent which is poorly soluble in said liquid, wherein the crystalline agent particles have an effective average particle size of less than about 1000 nm; and

(2) about 0.1 to 90% (w/w) of at least one surface modifier, based upon the combined weight of the surface modifier and the therapeutic agent, adsorbed on the surface of the crystalline therapeutic agent particles; and

(b) administering said aerosol to the lungs of said mammal.

The prior art cited above teach all the limitations of the claimed invention.

Instant invention is generically taught by the prior art.

It would have been obvious to one skilled in the art to prepare additional beneficial composition for the delivery and/or treatment of respiratory system by using the composition of the crystalline drug such as steroid containing particles of size less than 1000 nm because surface modifiers, droplets and crystalline particles of less than 1000 nm are taught by the prior art cited above. Instant invention would have been obvious at the time of invention because surface modifiers are used, the sizes of the nanoparticles are less than 1000 nm, and aerosols are droplets.

In the absence of a showing of criticality, of unobviousness or unexpected results over the prior art, the instant invention is considered obvious over the prior art for the reasons cited above.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sabiha Qazi whose telephone number is 703-305-3910. The examiner can normally be reached on every business day.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on 703-308-2927. The fax phone number for the organization where this application or proceeding is assigned is 703-308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

S. Qazi

SABIHA QAZI, PH.D
PRIMARY EXAMINER